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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,183	05/31/2001	James N. Higginbotham	P04580US1	9947
22885	7590	01/30/2004	EXAMINER	
MCKEE, VOORHEES & SEASE, P.L.C. 801 GRAND AVENUE SUITE 3200 DES MOINES, IA 50309-2721			GUZO, DAVID	
		ART UNIT	PAPER NUMBER	
		1636		

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/871,183	HIGGINBOTHAM ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 22 September 2003.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-46 is/are pending in the application.
4a) Of the above claim(s) 37-42 is/are withdrawn from consideration.
5) Claim(s) _____ is/are allowed.
6) Claim(s) 1-36 and 43-46 is/are rejected.
7) Claim(s) _____ is/are objected to.
8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). ____ .
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ . 6) Other: *Document on Petition re: Color drawings*

Detailed Action

Claims 37-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-15, 17 and 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Alemany et al.

Applicants' amendment has necessitated the withdrawal of the rejection against the method claims; however, this rejection is maintained against the composition (and cell) claims for reasons of record in the previous Office Action (Paper #9) and for reasons outlined below. Also, the rejection is extended to claim 17 as a result of applicants' amendment.

Applicants have responded to this rejection by amending claim 14 to recite that each vector is "...**capable of** (emphasis added) sustained viral replication and **capable of** (emphasis added) being produced independently in a separate trans-complementing packaging cell line, thereby providing individual higher titers than transcomplementing vectors that are produced co-dependently on the same packaging cell line." Applicants

then argue that Alemany et al. does not teach the newly recited limitations. Specifically, applicants assert that Alemany et al. only achieve titers of 10 TU/cell from a single packaging cell line co-transfected with both vectors while applicants achieve titers of 500 TU/cell when the vectors are produced independently in packaging cell lines.

Applicant's arguments filed 9/22/03 have been fully considered but they are not persuasive. Use of the phrase "capable of" with regard to the recited vectors does not differentiate the claimed vectors from the prior art wherein the vectors of the prior art **are also capable of** exhibiting the same characteristics. Additionally, under these circumstances, use of the phrase "capable of" without any context concerning under what circumstances the vectors are capable of exhibiting the recited characteristics and under what circumstances the vectors are not capable of exhibiting the recited characteristics does not differentiate the amended claims from the prior art. With regard to the phrase "...capable of sustained expression...", it is noted that applicants do not define the subjective term "sustained expression" and hence the duration of expression can potentially be any level of expression.

The vectors recited by Alemany et al. are capable of being produced independently of each other in separate trans-complementing packaging cell lines. For example, the GT5610 and AdH β vectors recited by Alemany et al. are each **capable of** being produced independently in any cell line(s) capable of expressing or being transfected with a vector expressing the adenoviral functions missing from either vector. The titers of the vectors produced would depend on the choice of the cell lines since some cell lines produce higher titers of vectors compared with other cell lines. It is

noted that the titers of vectors which could be obtained by producing the vectors independently in cell lines of choice does not add a patentably distinct limitation to the claimed composition because the claims do not recite titers of the vectors in the claimed composition and the titers of the vectors produced by any given packaging cell line are often more a property of the cell line and not the vector. As for applicants indication that they produced adenoviral vector titers of 500 TU/cell, it is unclear what cell line(s) were used to produce these titers and where in the specification support can be found for this assertion. It is again noted that the claimed invention consists of a composition of first and second viral vectors which are replication incompetent cotranscomplements of each other. Alemany et al. clearly teaches such a composition.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 13-17, 30-34, 44 and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Perricaudet et al.

This rejection is maintained for reasons of record in the previous Office Action and for reasons outlined below. The rejection is expanded to include claims 44 and 46 as a result of applicants' amendment filed 9/22/03. Applicants' amendment and

arguments are sufficient to overcome the rejection over the previously rejected method claims.

Applicants traverse this rejection by amending the claims as recited in the response to the above 35 USC 102(b) rejection over Alemany et al. Applicants assert that Perricaudet et al. does not show vectors whose replication is sustained and that Perricaudet et al. does not show sustained viral transcomplementation as the transcomplementing helper virus recited by Perricaudet et al. is not a replication competent vector and the defective replication functions of the helper cannot be transcomplemented by the defective recombinant adenoviral vector.

Applicants' arguments have been considered but are not persuasive. Applicants' arguments appear to be based upon reading limitations into the claims which are not present in said claims. For example, the use of the phrase concerning vectors which are "capable of sustained viral replication" reads on vectors which are capable of sustained replication under any circumstances and is not limited to sustained replication in any specific recipient cell, as applicants appear to assert. Also, the specification does not define what "sustained replication" encompasses and therefore this can read on practically any level of replication. Clearly, the vectors recited by Perricaudet et al. **are capable of sustained replication** if they are replicated in a packaging cell which complements *in trans* for the deficiencies in each of said vectors.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-36 and 43-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants have amended the independent claims (1, 14, 20, 31) to recite that the two (or more) vectors are "...capable of sustained replication..." and are "...capable of being produced independently of each other in separate trans-complementing packaging cell lines, thereby providing individual higher titers than vectors that are produced co-dependently on the same packaging cell line." There is no support in the specification for these broad limitations. While applicants apparently have support for a specific recombinant adenoviral vector combination (recombinant 1014 and AVC2.TK) wherein each vector is apparently produced in separate packaging cell lines, the specification provides no support for a generic teaching for any vector combination with these characteristics and the specification provides no support for vectors "capable of sustained replication". Additionally, the specification provides no support for producing higher vector titers from generation of each vector independently in separate packaging cell lines compared to titers generated from co-dependently producing the vectors in the same packaging cell line.

The specification also provides no support for methods or compositions comprising any adenoviral vectors with any **mutually excluding mutations** in two or

more genes selected from the group of E1, E2, E4, L1, L2, L3, L4 and L5. The specification provides no support for methods of increasing nucleotide transfer and expression in recipient cells or vector compositions with the newly recited vector limitations (i.e. capable of sustained viral replication, capable of producing higher titers when produced independently in separate packaging cell lines vs. co-dependently produced in a single cell line, etc.) wherein said methods comprise generation of (and use of) retroviral vectors, herpes viral vectors, AAV vectors, lentiviral vectors, EBV vectors and reoviral vectors.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 and 43-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 14, 20 and 31 (and dependent claims) are vague in the recitation of the phrase "...capable of **sustained** (emphasis added) replication..." or "...capable of **sustained** (emphasis added) viral replication...". The term "sustained replication" or "sustained viral replication" in claims 1, 14, 20 and 31 is a relative term which renders the claim indefinite. The term "sustained replication" or "sustained viral replication" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Additionally, these claims are vague in that

applicants recite a comparison between higher individual vector titers produced in separate trans-complementing cell lines vs. titers "...produced co-dependently in the **same packaging cell line** (emphasis added). It is unclear if the "same packaging cell line" refers to the same cell line as used to produce the vectors individually or to any cell line. It is noted that the limitation of "...produced independently of each other in separate trans-complementing packaging cell lines..." reads on the separate packaging cell lines being the same or different.

Any rejections not repeated in this Office Action are withdrawn.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
December 11, 2003


DAVID GUZO
PRIMARY EXAMINER